10593034

STRUCTURE FILE UPDATES: 7 SEP 2011 HIGHEST RN 1329744-16-2
DICTIONARY FILE UPDATES: 7 SEP 2011 HIGHEST RN 1329744-16-2

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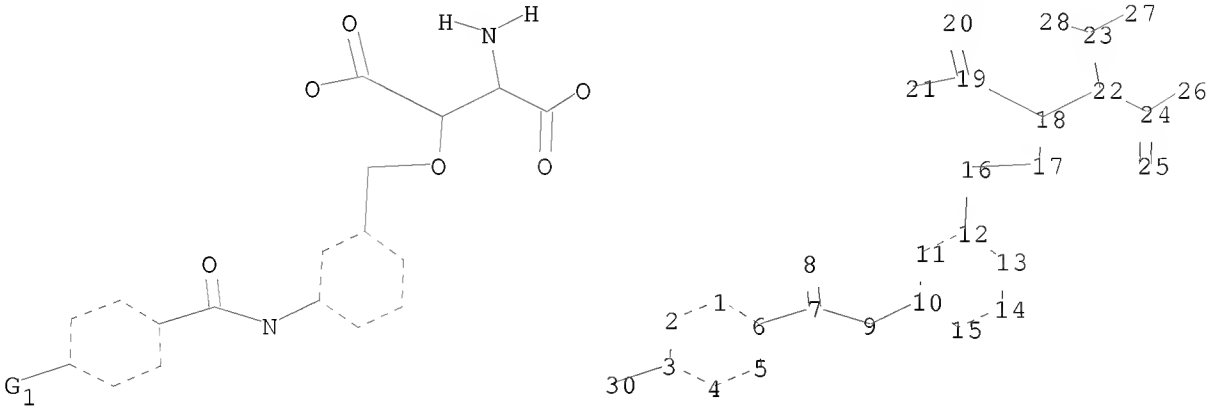
Uploading C:\Users\mbarker1\Documents\e-Red Folder\10593034\STN1.str



chain nodes :
7 8 9 16 17 18 19 20 21 22 23 24 25 26 27 28 30
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15
chain bonds :
3-30 6-7 7-8 7-9 9-10 12-16 16-17 17-18 18-19 18-22 19-20 19-21 22-23 22-24 23-27 23-28 24-25 24-26
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15
exact/norm bonds :
1-2 1-6 2-3 3-4 3-30 4-5 5-6 7-8 7-9 9-10 10-11 10-15 11-12 12-13 13-14 14-15 16-17 17-18 19-20 19-21 22-23 24-25 24-26
exact bonds :
6-7 12-16 18-19 18-22 22-24 23-27 23-28

G1:C,I

Match level :

EXR: Michael Barker

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1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 30:CLASS

L1 STRUCTURE UPLOADED

=> d
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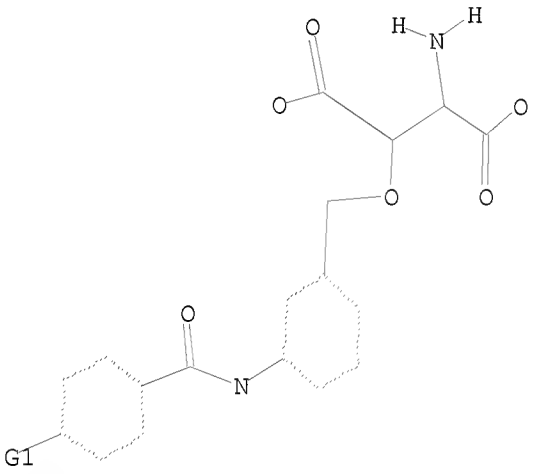
L1 STR



G1

G1:C,I

Structure attributes must be viewed using STN Express query preparation.

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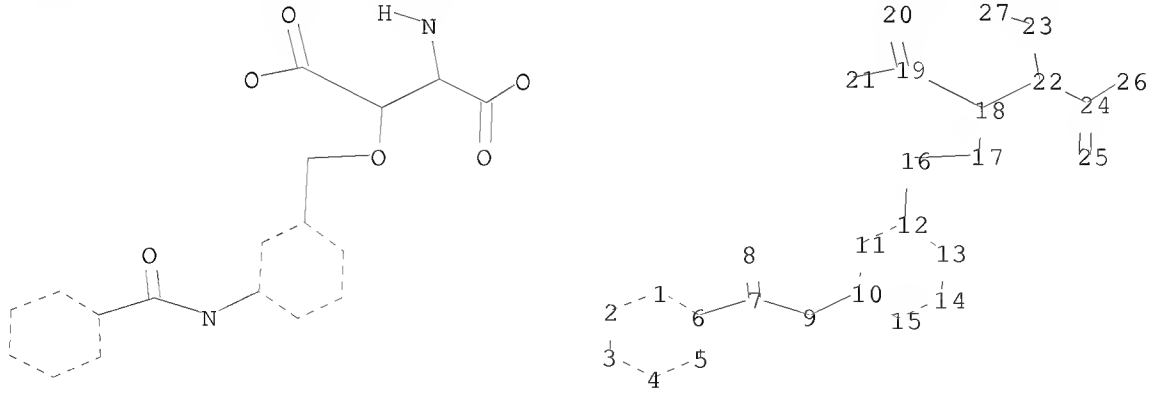


chain nodes :
7 8 9 16 17 18 19 20 21 22 23 24 25 26 27

EXR: Michael Barker

10593034

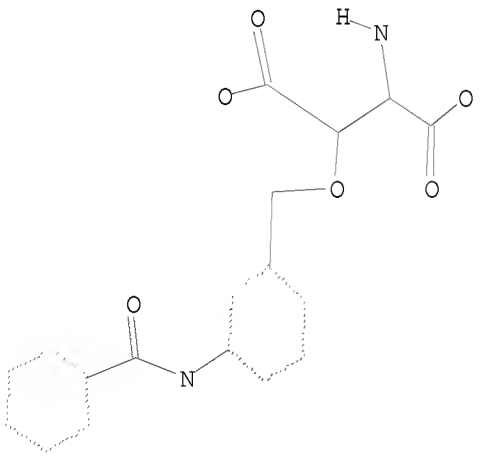
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15
chain bonds :
6-7 7-8 7-9 9-10 12-16 16-17 17-18 18-19 18-22 19-20 19-21 22-23 22-24
23-27 24-25 24-26
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-9 9-10 10-11 10-15 11-12 12-13 13-14
14-15 16-17 17-18 19-20 19-21 22-23 24-25 24-26
exact bonds :
6-7 12-16 18-19 18-22 22-24 23-27

G1:C,I

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS

L2 STRUCTURE UPLOADED

=> d
L2 HAS NO ANSWERS
L2 STR



G1:C,I

Structure attributes must be viewed using STN Express query preparation.

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FULL SEARCH INITIATED 15:25:43 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 50 TO ITERATE

EXR: Michael Barker

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100.0% PROCESSED 50 ITERATIONS 16 ANSWERS
SEARCH TIME: 00.00.01

L3 16 SEA SSS FUL L1

=> s l2 full
FULL SEARCH INITIATED 15:25:46 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 187 TO ITERATE

100.0% PROCESSED 187 ITERATIONS 42 ANSWERS
SEARCH TIME: 00.00.01

L4 42 SEA SSS FUL L2

=> fil caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 393.72 393.95

FILE 'CAPLUS' ENTERED AT 15:25:57 ON 08 SEP 2011
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 8 Sep 2011 VOL 155 ISS 11
FILE LAST UPDATED: 7 Sep 2011 (20110907/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2011
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2011

CAplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2011.

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L5 12 L3

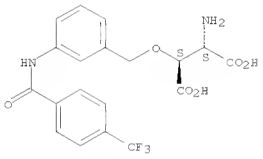
=> d ibib hitstr abs 1-12

EXR: Michael Barker

10593034

L5 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2010:168084 CAPLUS
DOCUMENT NUMBER: 152:279363
TITLE: Inhibitory effects of (2S, 3S)-3-[3-[4-(trifluoromethyl)benzoylamino]benzyloxy]aspartate (TFB-TBOA) on the astrocytic sodium responses to glutamate
AUTHOR(S): Bozzo, Luigi; Chatton, Jean-Yves
CORPORATE SOURCE: Department of Physiology, University of Lausanne, Switz.
SOURCE: Brain Research (2010), 1316, 27-34
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 480439-73-4, TFB-TBOA
RL: PAC (Pharmacological activity); BIOL (Biological study)
(inhibitory effects of (2S, 3S)-3-[3-[4-(trifluoromethyl)benzoylamino]benzyloxy]aspartate (TFB-TBOA) on astrocytic sodium responses to glutamate)
RN 480439-73-4 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

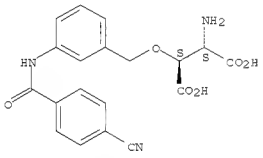
Absolute stereochemistry.



AB Astrocytes are responsible for the majority of the clearance of extracellular glutamate released during neuronal activity. DL-Threo-β-benzyloxyaspartate (TBOA) is extensively used as inhibitor of glutamate transport activity, but suffers from relatively low affinity for the transporter. Here, we characterized the effects of (2S, 3S)-3-[3-[4-(trifluoromethyl)benzoylamino]benzyloxy]aspartate (TFB-TBOA), a recently developed inhibitor of the glutamate transporter on mouse cortical astrocytes in primary culture. The glial Na+-glutamate transport system is very efficient and its activation by glutamate causes rapid intracellular Na+ concentration (Na+ i) changes that enable real time monitoring of transporter activity. Na+i was monitored by fluorescence microscopy in single astrocytes using the fluorescent Na+-sensitive probe sodium-binding benzofuran isophtalate. When applied alone, TFB-TBOA, at a concn. of 1 μM, caused small alterations of Na+i. TFB-TBOA inhibited the Na+i response evoked by 200 μM glutamate in a concn.-dependent manner with IC50 value of 43 ± 9 nM, as measured on the amplitude of the Na+i response. The max. inhibition of glutamate-evoked Na+i increase by TFB-TBOA was > 80%, but was only partly reversible. The residual response persisted in the presence of the AMPA/kainate receptor antagonist CNQX. TFB-TBOA also efficiently inhibited Na+i elevations caused by the application of D-aspartate, a transporter substrate that does not activate non-NMDA ionotropic receptors. TFB-TBOA was found not to influence the membrane properties of cultured cortical neurons recorded in whole-cell patch clamp. Thus, TFB-TBOA, with its high potency and its apparent lack of neuronal effects, appears to be one of the most useful pharmacol. tools available so far for studying glial glutamate transporters.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2008:526914 CAPLUS
DOCUMENT NUMBER: 149:97846
TITLE: Fragmental modeling of human glutamate transporter EAAT1 and analysis of its binding modes by docking and pharmacophore mapping
AUTHOR(S): Pedretti, Alessandro; De Luca, Laura; Sciarrillo, Cristina; Vistoli, Giulio
CORPORATE SOURCE: Istituto di Chimica Farmaceutica e Tossicologica "Pietro Pratesi", Facolta di Farmacia, Universita degli Studi di Milano, Milan, I-20133, Italy
SOURCE: ChemMedChem (2008), 3(1), 79-90
CODEN: CHEMGX; ISSN: 1860-7179
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 480439-69-8 480439-73-4, TFB-TBOA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fragmental modeling of human glutamate transporter EAAT1 and anal. of its binding modes by docking and pharmacophore mapping)
RN 480439-69-8 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-cyanobenzoyl)amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 480439-73-4 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

AB The objective of the study was to generate a reliable model of the homotrimeric structure for the human glutamate transporter EAAT1, based on exptl. folding of transporter homolog from Pyrococcus horikoshii. The monomer structure was derived using a fragmental approach and the homotrimer was assembled using protein-protein docking. The interaction capacities of the EAAT1 model were explored by docking a set of 32 known ligands including both substrates and blockers. Docking results unveiled that the substrates' bioactivity is strongly influenced by a precise fitting between the ligand and the EAAT1 binding site, whereas the blockers' activity depends on a set of apolar contacts that ligands can realize in an adjacent hydrophobic subpocket. The docking results were further verified by generating two pharmacophore models (the first for substrates and the latter for blockers) which revealed the features necessary for high EAAT1 activity. The consistency of docking results and the agreement with pharmacophore models afford an encouraging validation for the EAAT1 model and emphasize the soundness of the fragmental approach to model any transmembrane protein.
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

EXR: Michael Barker

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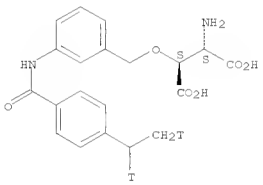
L5 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2007:22602 CAPLUS
DOCUMENT NUMBER: 146:244722
TITLE: Characterization of the tritium-labeled analog of L-threo-β-benzyloxyaspartate binding to glutamate transporters
AUTHOR(S): Shimamoto, Keiko; Otsubo, Yasuto; Shigeri, Yasushi; Yasuda-Kamatani, Yoshimi; Satoh, Masamichi; Kaneko, Shuji; Nakagawa, Takayuki
CORPORATE SOURCE: Suntory Institute for Bioorganic Research, Wakayamadai, Shimamoto-cho, Mishima-gun, Osaka, Japan
SOURCE: Molecular Pharmacology (2007), 71(1), 294-302
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 864937-05-3P
RL: ARG (Analytical reagent use); PKT (Pharmacokinetics); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(characterization of tritium-labeled analog of L-threo-β-benzyloxyaspartate binding to glutamate transporters)
RN 864937-05-3 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(ethyl-1,2-t2)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



AB L-Glutamate is the major excitatory neurotransmitter in the mammalian central nervous system. Termination of glutamate receptor activation and maintenance of low extracellular glutamate concns. are primarily achieved by glutamate transporters (excitatory amino acid transporters 1-5, EAATs 1-5) located on both the nerve endings and the surrounding glial cells. To identify the physiol. roles of each subtype, subtype-selective EAAT ligands are required. In this study, we developed a binding assay system to characterize EAAT ligands for all EAAT subtypes. We recently synthesized novel analogs of threo-β-benzyloxyaspartate (TBOA) and reported that they blocked glutamate uptake by EAATs 1-5 much more potently than TBOA. The strong inhibitory activity of the TBOA analogs

L5 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
suggested that they would be suitable to use as radioisotope-labeled ligands, and we therefore synthesized a tritiated deriv. of (2S,3S)-3-[3-[4-ethylbenzoylamino]benzyloxy]aspartate ([3H]ETB-TBOA). [3H]ETB-TBOA showed significant high-affinity specific binding to EAAT-transfected COS-1 cell membranes with each EAAT subtype. The Hill coeff. for the Na+-dependence of [3H]ETB-TBOA binding revealed a single class of noncooperative binding sites for Na+, suggesting that Na+ binding
in the ligand binding step is different from Na+ binding in the substrate uptake process. The binding was displaced by known substrates and blockers. The rank order of inhibition by these compds. was consistent with glutamate uptake assay results reported previously. Thus, the [3H]ETB-TBOA binding assay will be useful to screen novel EAAT ligands for
all EAAT subtypes.
OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD
(6 CITINGS)
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2006:656062 CAPLUS
DOCUMENT NUMBER: 145:124841
TITLE: Preparation of β-benzyloxyaspartic acid derivatives as affinity-column ligands and glutamic acid transporter inhibitors
INVENTOR(S): Shimamoto, Keiko
PATENT ASSIGNEE(S): Suntory Limited, Japan
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006070737	A1	20060706	WO 2005-JP23773	20051226
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
JP 2006182696	A	20060713	JP 2004-377557	20041227
JP 4008446	B2	20071114		
EP 1849766	A1	20071031	EP 2005-820230	20051226
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
US 20080070321	A1	20080320	US 2007-794124	20070626
US 7670784	B2	20100302		
PRIORITY APPLN. INFO.:			JP 2004-377557 A	20041227
			WO 2005-JP23773 W	20051226

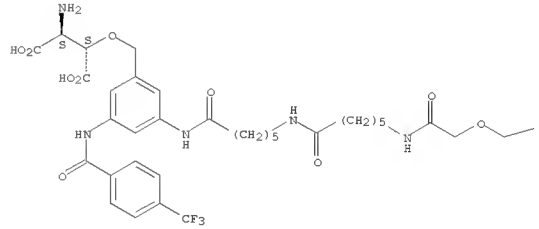
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 145:124841
IT 896712-90-6P 896712-92-8P 896712-94-0P
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of β-benzyloxyaspartic acid derivs. as affinity-column ligands and glutamic acid transporter inhibitors)
RN 896712-90-6 CAPLUS
CN L-Aspartic acid, 3-[[3-[(28-amino-1,8,15-trioxo-17,20,23,26-tetraoxa-7,14-diazaoctacos-1-yl)amino]-5-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

L5 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
CRN 896712-89-3
CMF C41 H59 F3 N6 O13

Absolute stereochemistry. Rotation (-).

PAGE 1-A



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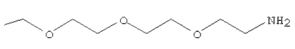

CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 896712-92-8 CAPLUS
CN L-Aspartic acid, 3-[[3,5-bis[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)-,

EXR: Michael Barker

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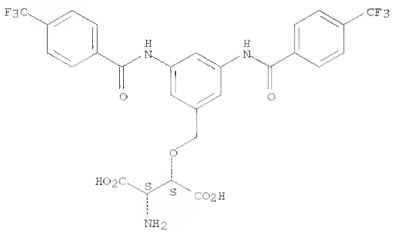
L5 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 896712-91-7
CMF C27 H21 F6 N3 O7

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

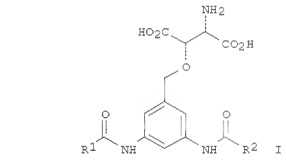
RN 896712-94-0 CAPLUS
CN L-Aspartic acid, 3-[[3-[(1-oxopropyl)amino]-5-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

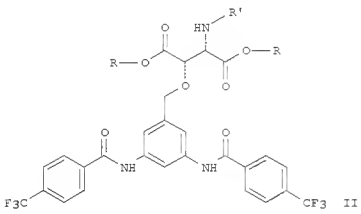
CRN 896712-93-9
CMF C22 H22 F3 N3 O7

Absolute stereochemistry.

L5 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



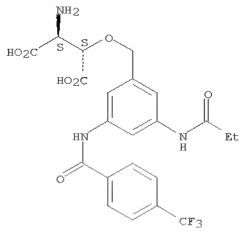
I



II

AB Title compds. I [R1 = (un)substituted aromatic group; R2 = (un)substituted linear or branched aliphatic group optionally having nitrogen or oxygen in the chain, (un)substituted aromatic group] and salts thereof were prepared For example, treatment of compound II [R = tert-butyl; R' = tert-butoxycarbonyl] with trifluoroacetic acid afforded compound II [R, R' = H] trifluoroacetic acid salt in 84% yield. In glutamic acid uptake inhibition assays, IC50 values of compound II [R, R' = H]·CF3CO2H for EAAT2 and EAAT3 were 1.3 and 0.46 nM, resp. A method of purifying or detecting an L-glutamic acid transporter using compds. 1 is provided.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



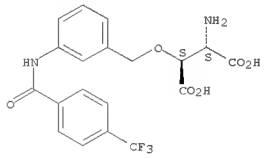
CM 2

CRN 76-05-1
CMF C2 H F3 O2

GI

L5 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2006:129293 CAPLUS
DOCUMENT NUMBER: 144:324958
TITLE: Elucidation of glutamate transporter functions using selective inhibitors
AUTHOR(S): Shimamoto, Keiko
CORPORATE SOURCE: Suntory Institute for Bioorganic Research, 1-1-1 Wakayamadai, Shimamoto-cho, Mishima-gun, Osaka, 618-8503, Japan
SOURCE: Shinkei Kenkyu no Shinpo (2005), 49(6), 850-854 CODEN: SKNSAF; ISSN: 0001-8724
PUBLISHER: Igaku Shoin Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
IT 480439-73-4, TFB-TBOA
RL: BSU (Biological study, unclassified); BIOL (Biological study) (elucidation of glutamate transporter functions using selective inhibitors)
RN 480439-73-4 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



AB A review. L-Glutamate is the major excitatory neurotransmitter in the mammalian central nervous system(CNS). To terminate glutamate receptor activation and to protect neurons from excitotoxicity, extracellular glutamate concns. are strictly controlled by sodium dependent glutamate transporters (excitatory amino acid transporters 1-5 : EAATs1-5) located in nerve endings and surrounding glia cells. Selective and potent inhibitors have served as important exptl. tools to identify the physiol. roles of transporters in the regulation of synaptic transmission or in the pathogenesis of neurol. diseases. A pharmacol. useful probe, threo-β-benzyloxyaspartate (DL-TBOA) which functions as a non-transportable blocker for all subtypes of EAATs, has emerged from modification of a known inhibitor threo-β-hydroxyaspartate (THA). Non-transportable blockers are indispensable because, unlike substrates, they do not cause heteroexchange. By comparing the effects of substrates and non-transportable blockers, physiol. roles of EAATs have been revealed. EAATs not only remove transmitter from synaptic clefts but also actively modulate neurotransmission. Moreover, higher affinity ligands have been developed as novel pharmacol. tools. TBOA analogs possessing a bulky substituent on their benzene ring significantly inhibited labeled

EXR: Michael Barker

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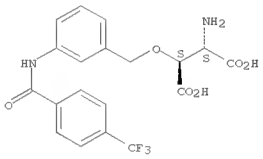
L5 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
glutamate uptake, the most potent of compd. being (2S, 3S)-3-{3-[4-(tri-fluoromethyl) benzoyl-amino] benzyloxy} aspartate (TFB-TBOA). TFB-TBOA is genuinely non-transportable at ED and showed no effects on glutamate receptors. TFB-TBOA would be a suitable lead compd. for designing functionalized ligands from the perspective of its markedly high affinity for EAAT proteins.

L5 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2006:24201 CAPLUS
DOCUMENT NUMBER: 144:142897
TITLE: Facilitative effect of a glutamate transporter inhibitor (2S,3S)-3-{3-[4-(trifluoromethyl)benzoylamino]benzyloxy}aspartate on the expression of methamphetamine-induced behavioral sensitization in rats
AUTHOR(S): Fujio, Mayumi; Nakagawa, Takayuki; Suzuki, Yuichi; Satoh, Masamichi; Kaneko, Shuji
CORPORATE SOURCE: Department of Molecular Pharmacology, Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan
SOURCE: Journal of Pharmacological Sciences (Tokyo, Japan) (2005), 99(4), 415-418
CODEN: JPSTGJ; ISSN: 1347-8613
PUBLISHER: Japanese Pharmacological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 480439-73-4
RL: PAC (Pharmacological activity); BIOL (Biological study)
(facilitative effect of a glutamate transporter inhibitor {[(trifluoromethyl)benzoylamino]benzyloxy}aspartate on expression of methamphetamine-induced behavioral sensitization in rats)
RN 480439-73-4 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



AB We examined the effects of a potent glutamate transporter inhibitor, (2S,3S)-3-{3-[4-(trifluoromethyl)benzoylamino]benzyloxy}aspartate (TFB-TBOA), on the expression of methamphetamine-induced behavioral sensitization in rats. Rats were i.p. treated with 2 mg/kg methamphetamine for 5 days and then challenged with 1 mg/kg methamphetamine. Intracerebroventricular administration of TFB-TBOA (0.1 nmol) 10 min before the challenge significantly facilitated the expression of behavioral sensitization. It had no effect on the locomotor activation elicited by the challenge with methamphetamine in repeated-saline-treated

L5 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
(non-sensitized) rats. These results suggest that central glutamate transporters may play an inhibitory role in the expression of behavioral sensitization to methamphetamine.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2005:1042190 CAPLUS
DOCUMENT NUMBER: 143:306541
TITLE: Preparation of radiolabeled 3-[3-(benzoylamino)benzyloxy]aspartic acid derivatives as glutamate transporter inhibitors
INVENTOR(S): Shimamoto, Keiko; Saji, Hideo; Kuge, Yuji; Ueda, Masashi; Satoh, Masamichi; Nakagawa, Takayuki
PATENT ASSIGNEE(S): Suntory Limited, Japan
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005090268	A1	20050929	WO 2005-JP5600	20050318
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1732864	A1	20061220	EP 2005-721527	20050318
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007529412	T	20071025	JP 2006-529410	20050318
US 20080248485	A1	20081009	US 2006-593034	20060915
PRIORITY APPLN. INFO.:			JP 2004-79116	A 20040318
			WO 2005-JP5600	W 20050318

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 143:306541; MARPAT 143:306541
IT 864936-98-1P 864936-99-2P 864937-04-2P
RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of radiolabeled [(benzoylamino)benzyloxy]aspartic acid derivs. as glutamate transporter inhibitors)
RN 864936-98-1 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(iodo-125I)benzoyl]amino]phenyl]methoxy]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

EXR: Michael Barker

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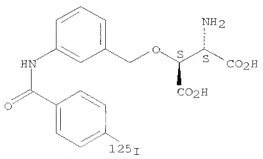
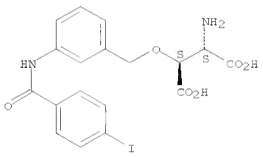
L5 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



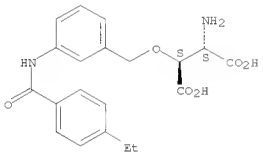
RN 864936-99-2 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-iodobenzoyl)amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 864937-04-2 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-ethylbenzoyl)amino]phenyl]methoxy]-, (3S)- (CA
INDEX NAME)

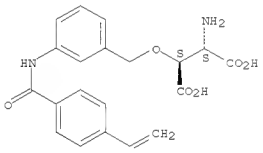
Absolute stereochemistry.



IT 480439-73-4 864937-05-3D, tritium-labeled

L5 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)

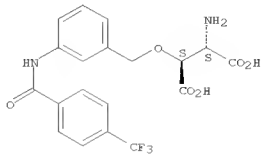
Absolute stereochemistry.



AB The invention provides a radiolabeled ligand which is highly selective and
potent for glutamate transporters and is usable in specifically detecting the glutamate transporter. Specifically, the invention provides 3-[3-(benzoylamino)benzyloxy]aspartic acid (BzA-TBOA) having a radioactive
substituent at the p-position of the benzoyl group, as well as esters or salts. Thus, [125I]I-BzA-TBOA was prepared from N,O-protected A-TBOA by acylation with 4-bromobenzoyl chloride, tributylstannylation, substitution
reaction with Na125I, and deprotection. Glutamate transporter inhibitory activity data are tabulated for compds. of the invention.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

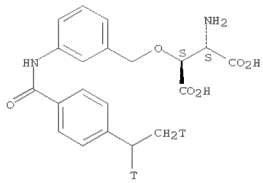
L5 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of radiolabeled [(benzoylamino)benzyloxy]aspartic acid derivs. as glutamate transporter inhibitors)
RN 480439-73-4 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 864937-05-3 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(ethyl-1,2-t2)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



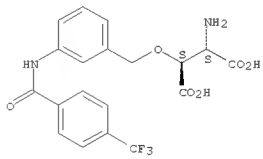
IT 864937-03-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of radiolabeled [(benzoylamino)benzyloxy]aspartic acid derivs.
as glutamate transporter inhibitors)
RN 864937-03-1 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-ethenylbenzoyl)amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

L5 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER:	2005:299120 CAPLUS
DOCUMENT NUMBER:	142:442183
TITLE:	A novel L-glutamate transporter inhibitor reveals endogenous D-aspartate homeostasis in rat pheochromocytoma MPT1 cells
AUTHOR(S):	Koyama, Hayato; Sekine, Masae; Furuchi, Takemitsu; Katane, Masumi; Nimura, Noriyuki; Shimamoto, Keiko; Nakajima, Terumi; Homma, Hiroshi
CORPORATE SOURCE:	School of Pharmaceutical Sciences, Kitasato University, Minato-ku, Tokyo, 108-8641, Japan
SOURCE:	Life Sciences (2005), 76(25), 2933-2944 CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER:	Elsevier B.V.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

IT 480439-73-4
RL: BUU (Biological use, unclassified); PAC (Pharmacological activity); BIOL (Biological study); USES (Uses)
(glutamate transporter inhibitor reveals endogenous D-aspartate homeostasis in rat pheochromocytoma MPT1 cells)
RN 480439-73-4 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



AB We previously reported for the first time that D-aspartate (D-Asp) is biosynthesized by cultured mammalian cells such as pheochromocytoma (PC)12
cells and its subclone MPT1 (FEBS Lett. 434 (1998) 231, Arch. Biochem. Biophys. 404 (2002) 92). We speculated that D-Asp levels in the intra- and extracellular spaces of the cultured cells are maintained in a dynamic
state of homeostasis. To test this here, we utilized a novel and potent L-Glu transporter inhibitor, (2S,3S)-3-[3-[4-(trifluoromethyl)benzyloylamino]benzyloxy]aspartate (TFB-TBOA). This inhibitor proved to be a genuine nontransportable blocker of the transporter even during long periods of culture. Use of this inhibitor with MPT1 cells confirmed that D-Asp levels are in a dynamic steady state where it is constantly released into the extracellular space by a yet undefined mechanism as well as being constantly and intensively taken up by the cells via the L-Glu transporter. We estimated the rate with which D-Asp is constitutively released from MPT1 cells is approx. 3.8 pmol/h/1 × 105 cells.

EXR: Michael Barker

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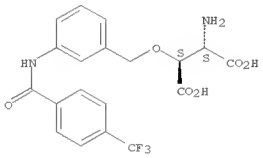
L5 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD
(7 CITINGS)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2005:214287 CAPLUS
DOCUMENT NUMBER: 143:146338
TITLE: Effects of a novel glutamate transporter blocker, (2S,3S)-3-{3-[4-(trifluoromethyl)benzoylamino]benzyloxy}aspartate (TFB-TBOA), on activities of hippocampal neurons
AUTHOR(S): Tsukada, Shota; Iino, Masae; Takayasu, Yukihiro; Shimamoto, Keiko; Ozawa, Seiji
CORPORATE SOURCE: Department of Neurophysiology, Gunma University Graduate School of Medicine, 3-39-22 Showa-machi, Maebashi, Gunma, 371-8511, Japan
SOURCE: Neuropharmacology (2005), 48(4), 479-491
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 480439-73-4, TFB-TBOA
RL: PAC (Pharmacological activity); BIOL (Biological study)
(effects of a novel glutamate transporter blocker, (2S,3S)-3-{3-[4-(trifluoromethyl)benzoylamino]benzyloxy}aspartate (TFB-TBOA), on activities of hippocampal neurons)
RN 480439-73-4 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

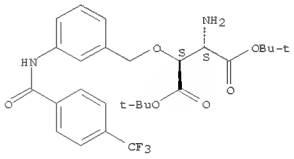


AB Glutamate transporters rapidly take up synaptically released glutamate and
maintain the glutamate concentration in the synaptic cleft at a low level. (2S,
3S)-3-{3-[4-(trifluoromethyl)benzoylamino]benzyloxy}aspartate (TFB-TBOA) is a novel glutamate transporter blocker that potently suppresses the activity of glial transporters. TFB-TBOA inhibited synaptically activated
transporter currents (STCs) in astrocytes in the stratum radiatum in rat hippocampal slices in a dose-dependent manner with an IC50 of 13 nM, and reduced them to approx. 10% of the control at 100 nM. We investigated the
effects of TFB-TBOA on glutamatergic synaptic transmission and cell

L5 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
excitability in CA1 pyramidal cells. TFB-TBOA (100 nM) prolonged the decay of N-methyl--aspartic acid receptor (NMDAR)-mediated excitatory postsynaptic currents (EPSCs), whereas it prolonged that of α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR)-mediated EPSCs only when the desensitization of AMPARs was reduced
by cyclothiazide (CTZ). Furthermore, long-term application of TFB-TBOA induced spontaneous epileptiform discharges with a continuous depolarization shift of membrane potential. These epileptiform activities
were mainly attributed to NMDAR activation. Even after pharmacol. block of NMDARs, however, TFB-TBOA induced similar changes by activating AMPARs in the presence of CTZ. Thus, the continuous uptake of synaptically released glutamate by glial transporters is indispensable for protecting hippocampal neurons from glutamate receptor-mediated hyperexcitabilities.
OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2004:469790 CAPLUS
DOCUMENT NUMBER: 141:184585
TITLE: Synthesis of carbamate-type caged derivatives of a novel glutamate transporter blocker
AUTHOR(S): Takaoka, Kiyo; Tatsu, Yoshiro; Yumoto, Noboru; Nakajima, Terumi; Shimamoto, Keiko
CORPORATE SOURCE: Suntory Institute for Bioorganic Research, 1-1-1 Wakayamadai, Osaka, Shimamoto, 618-8503, Japan
SOURCE: Bioorganic & Medicinal Chemistry (2004), 12(13), 3687-3694
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:184585
IT 737830-21-6P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of carbamate-type caged derivs. of novel glutamate transporter blocker)
RN 737830-21-6 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, bis(1,1-dimethylethyl) ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB L-threo-β-Benzyloxyaspartate (l-TBOA) and (2S,3S)-3-{3-[4-(trifluoromethyl)benzoylamino]benzyloxy}aspartate (L-TFB-TBOA) are potent nontransportable blockers for glutamate transporters. The authors synthesized a carbamate-type coumarin derivative of
L-TBOA (3a) as a caged blocker and compared 3a with the corresponding ester-type analogs 1. The carbamate 3a was less sensitive to photolysis than the ester 1 but was more stable in the aqueous solution The [6,7-bis(carboxymethoxy)-coumarin-4-yl]methylcarbonyl (BCMCMC) group exhibited good results both in photoreactivity and stability. Therefore, the authors examined photolysis of N-BCMCMC-TBOA and N-BCMCMC-TFB-TBOA, which immediately released blockers to show glutamate uptake inhibition.
OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

EXR: Michael Barker

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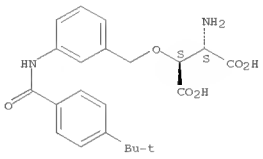
L5 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)

L5 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2004:292674 CAPLUS
DOCUMENT NUMBER: 141:16890
TITLE: Characterization of novel L-threo-β-benzyloxyaspartate derivatives, potent blockers of the glutamate transporters
AUTHOR(S): Shimamoto, Keiko; Sakai, Ryuichi; Takaoka, Kiyo; Yumoto, Noboru; Nakajima, Terumi; Amara, Susan G.; Shigeri, Yasushi
CORPORATE SOURCE: Suntory Institute for Bioorganic Research, Osaka, 618-8503, Japan
SOURCE: Molecular Pharmacology (2004), 65(4), 1008-1015
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 479690-57-8 480439-69-8 480439-73-4
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(characterization of novel L-threo-β-benzyloxyaspartate derivs., potent blockers of glutamate transporters)
RN 479690-57-8 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

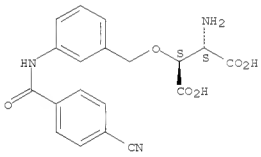
Absolute stereochemistry.



RN 480439-69-8 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-cyanobenzoyl)amino]phenyl]methoxy]-, (3S)- (CA
INDEX NAME)

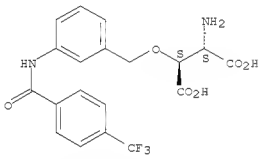
Absolute stereochemistry.

L5 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



RN 480439-73-4 CAPLUS
CN L-Aspartic acid,
3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-
, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



AB Nontransportable blockers of the glutamate transporters are important tools for investigating mechanisms of synaptic transmission. DL-threo-β-Benzyloxyaspartate (DL-TBOA) is a potent blocker of all subtypes of the excitatory amino acid transporters (EAATs). We characterized novel L-TBOA analogs possessing a substituent on their resp.
benzene rings. The analogs significantly inhibited labeled glutamate uptake, the most potent of which was (2S,3S)-3-{3-[4-(trifluoromethyl)benzoylamino]benzyloxy}aspartate (TFB-TBOA). In an uptake assay using cells transiently expressing EAATs, the IC50 values of TFB-TBOA for EAAT1, EAAT2, and EAAT3 were 22, 17, and 300 nM, resp. TFB-TBOA was significantly more potent at inhibiting EAAT1 and EAAT2 compared with L-TBOA (IC50 values for EAAT1-3 were 33, 6.2, and 15 μM, resp.). Electrophysiol. analyses revealed that TBOA analogs block the transport-associated currents in all five EAAT subtypes and also
block leak currents in EAAT5. The rank order of the analogs for potencies
at inhibiting substrate-induced currents was identical to that observed in
the uptake assay. However, the kinetics of TFB-TBOA differed from the kinetics of L-TBOA, probably because of the strong binding affinity. Notably, TFB-TBOA did not affect other representative neurotransmitter transporters or receptors, including ionotropic and metabotropic glutamate
receptors, indicating that it is highly selective for EAATs. Moreover, intracerebroventricular administration of the TBOA analogs induced severe convulsive behaviors in mice, probably because of the accumulation of glutamate. Taken together, these findings indicate that novel TBOA analogs, esp. TFB-TBOA, should serve as useful tools for elucidating the physiol. roles of the glutamate transporters.
OS.CITING REF COUNT: 44 THERE ARE 44 CAPLUS RECORDS THAT CITE THIS RECORD (44 CITINGS)
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

EXR: Michael Barker

10593034

L5 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2003:5966 CAPLUS
DOCUMENT NUMBER: 138:72990
TITLE: Preparation of β-(aminobenzyloxy)aspartate derivatives as glutamate transporter inhibitors
INVENTOR(S): Shimamoto, Keiko
PATENT ASSIGNEE(S): Suntory Limited, Japan
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000698	A1	20030103	WO 2002-JP6286	20020624
W: AU, BR, CA, CN, IL, JP, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
AU 2002345364	A1	20030108	AU 2002-345364	20020624
EP 1397370	A1	20040317	EP 2002-743696	20020624
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2005504016	T	20050210	JP 2003-507101	20020624
JP 4542336	B2	20100915		
US 20040242652	A1	20041202	US 2004-481237	20040719
US 7247652	B2	20070724		
US 20070238783	A1	20071011	US 2007-808970	20070614
US 7666906	B2	20100223		

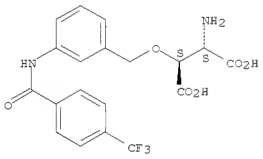
PRIORITY APPLN. INFO.:
JP 2001-190022 A 20010622
WO 2002-JP6286 W 20020624
US 2004-481237 A3 20040719

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 138:72990; MARPAT 138:72990
IT 479690-57-8P, TBu-BzA-TBOA 479690-58-9P
480439-69-8P, CN-Bza-TBOA 480439-73-4P, CF3-Bza-TBOA
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (aminobenzyloxy)aspartate derivs. as glutamate transporter
inhibitors)
RN 479690-57-8 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



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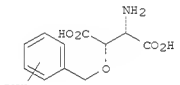
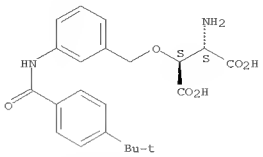


RNH I

AB L-Threo-β-benzyloxyaspartate derivs. I [R = H, (un)substituted acyl, an amino acid- or biotin-derived group] or their salts were prepared for binding to affinity column chromatog. carriers as ligands of glutamate transporter proteins. Thus, I (R = m-H2NCH2CH2CONH) (AA-TBOA) was prepared
by a multistep synthesis starting with the reaction of (2S,3R)-[3-(benzyloxymethyl)oxiranyl]methyl p-nitrobenzoate with benzoyl isocyanate. The inhibitory effect of AA-TBOA was determined to be IC50 = 2.1
± 0.1 μM and 7.9 ± 0.76 μM, resp., for uptake of (14)glutamate by human EAAT2 or EAAT3 stably expressed on MDCK cells or transiently expressed on COS-1 cells.
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD
(6 CITINGS)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



RN 479690-58-9 CAPLUS
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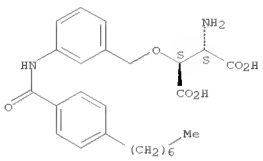
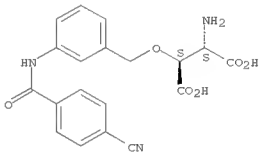
Absolute stereochemistry.



RN 480439-69-8 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-cyanobenzoyl)amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 480439-73-4 CAPLUS

EXR: Michael Barker

10593034

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L6           13 L4

=> d ibib abs hitstr 1-13
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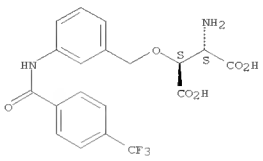
EXR: Michael Barker

10593034

L6 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2010:168084 CAPLUS
DOCUMENT NUMBER: 152:279363
TITLE: Inhibitory effects of (2S, 3S)-3-[3-[4-(trifluoromethyl)benzoylamino]benzyloxy]aspartate (TFB-TBOA) on the astrocytic sodium responses to glutamate
AUTHOR(S): Bozzo, Luigi; Chatton, Jean-Yves
CORPORATE SOURCE: Department of Physiology, University of Lausanne, Switz.
SOURCE: Brain Research (2010), 1316, 27-34
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Astrocytes are responsible for the majority of the clearance of extracellular glutamate released during neuronal activity. DL-Threo-β-benzyloxyaspartate (TBOA) is extensively used as inhibitor of glutamate transport activity, but suffers from relatively low affinity for the transporter. Here, we characterized the effects of (2S, 3S)-3-[3-[4-(trifluoromethyl)benzoylamino]benzyloxy]aspartate (TFB-TBOA), a recently developed inhibitor of the glutamate transporter on mouse cortical astrocytes in primary culture. The glial Na+-glutamate transport system is very efficient and its activation by glutamate causes rapid intracellular Na+ concentration (Na+ i) changes that enable real time monitoring of transporter activity. Na+i was monitored by fluorescence microscopy in single astrocytes using the fluorescent Na+-sensitive probe sodium-binding benzofuran isophtalate. When applied alone, TFB-TBOA, at a concentration of 1 μM, caused small alterations of Na+i. TFB-TBOA inhibited the Na+i response evoked by 200 μM glutamate in a concentration-dependent manner with IC50 value of 43 ± 9 nM, as measured on the amplitude of the Na+i response. The maximum inhibition of glutamate-evoked Na+i increase by TFB-TBOA was > 80%, but was only partly reversible. The residual response persisted in the presence of the AMPA/kainate receptor antagonist CNQX. TFB-TBOA also efficiently inhibited Na+i elevations caused by the application of D-aspartate, a transporter substrate that does not activate non-NMDA ionotropic receptors. TFB-TBOA was found not to influence the membrane properties of cultured cortical neurons recorded in whole-cell patch clamp. Thus, TFB-TBOA, with its high potency and its apparent lack of neuronal effects, appears to be one of the most useful pharmacol. tools available so far for studying glial glutamate transporters.
IT 480439-73-4, TFB-TBOA
RL: PAC (Pharmacological activity); BIOL (Biological study)
(inhibitory effects of (2S, 3S)-3-[3-[4-(trifluoromethyl)benzoylamino]benzyloxy]aspartate (TFB-TBOA) on

L6 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
astrocytic sodium responses to glutamate)
RN 480439-73-4 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

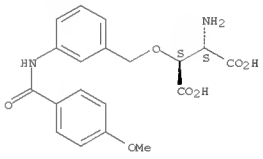


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2008:526914 CAPLUS
DOCUMENT NUMBER: 149:97846
TITLE: Fragmental modeling of human glutamate transporter EAAT1 and analysis of its binding modes by docking and pharmacophore mapping
AUTHOR(S): Pedretti, Alessandro; De Luca, Laura; Sciarrillo, Cristina; Vistoli, Giulio
CORPORATE SOURCE: Istituto di Chimica Farmaceutica e Tossicologica "Pietro Pratesi", Facolta di Farmacia, Universita degli Studi di Milano, Milan, I-20133, Italy
SOURCE: ChemMedChem [2008], 3(1), 79-90
CODEN: CHEMGX; ISSN: 1860-7179
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The objective of the study was to generate a reliable model of the homotrimeric structure for the human glutamate transporter EAAT1, based on exptl. folding of transporter homolog from Pyrococcus horikoshii. The monomer structure was derived using a fragmental approach and the homotrimer was assembled using protein-protein docking. The interaction capacities of the EAAT1 model were explored by docking a set of 32 known ligands including both substrates and blockers. Docking results unveiled that the substrates' bioactivity is strongly influenced by a precise fitting between the ligand and the EAAT1 binding site, whereas the blockers' activity depends on a set of apolar contacts that ligands can realize in an adjacent hydrophobic subpocket. The docking results were further verified by generating two pharmacophore models (the first for substrates and the latter for blockers) which revealed the features necessary for high EAAT1 activity. The consistency of docking results and the agreement with pharmacophore models afford an encouraging validation for the EAAT1 model and emphasize the soundness of the fragmental approach to model any transmembrane protein.
IT 480439-66-5 480439-69-8 480439-73-4, TFB-TBOA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fragmental modeling of human glutamate transporter EAAT1 and anal. of its binding modes by docking and pharmacophore mapping)
RN 480439-66-5 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-methoxybenzoyl)amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

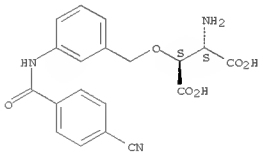
Absolute stereochemistry.

L6 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



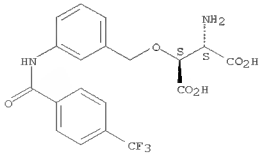
RN 480439-69-8 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-cyanobenzoyl)amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 480439-73-4 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS

EXR: Michael Barker

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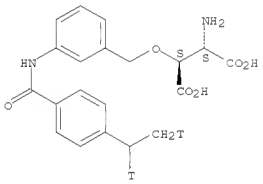
L6 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L6 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD
(6 CITINGS)
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L6 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2007:22602 CAPLUS
DOCUMENT NUMBER: 146:244722
TITLE: Characterization of the tritium-labeled analog of L-threo-β-benzyloxyaspartate binding to glutamate transporters
AUTHOR(S): Shimamoto, Keiko; Otsubo, Yasuto; Shigeri, Yasushi; Yasuda-Kamatani, Yoshimi; Satoh, Masamichi; Kaneko, Shuji; Nakagawa, Takayuki
CORPORATE SOURCE: Suntory Institute for Bioorganic Research, Wakayamadai, Shimamoto-cho, Mishima-gun, Osaka, Japan
SOURCE: Molecular Pharmacology (2007), 71(1), 294-302
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB L-Glutamate is the major excitatory neurotransmitter in the mammalian central nervous system. Termination of glutamate receptor activation and maintenance of low extracellular glutamate concns. are primarily achieved by glutamate transporters (excitatory amino acid transporters 1-5, EAATs 1-5) located on both the nerve endings and the surrounding glial cells. To identify the physiol. roles of each subtype, subtype-selective EAAT ligands are required. In this study, we developed a binding assay system to characterize EAAT ligands for all EAAT subtypes. We recently synthesized novel analogs of threo-β-benzyloxyaspartate (TBOA) and reported that they blocked glutamate uptake by EAATs 1-5 much more potently than TBOA. The strong inhibitory activity of the TBOA analogs suggested that they would be suitable to use as radioisotope-labeled ligands, and we therefore synthesized a tritiated derivative of (2S,3S)-3-{3-[4-ethylbenzoylamino]benzyloxy}aspartate ([3H]ETB-TBOA). [3H]ETB-TBOA showed significant high-affinity specific binding to EAAT-transfected COS-1 cell membranes with each EAAT subtype. The Hill coefficient for the Na+-dependence of [3H]ETB-TBOA binding revealed a single class of noncooperative binding sites for Na+, suggesting that Na+ binding in the ligand binding step is different from Na+ binding in the substrate uptake process. The binding was displaced by known substrates and blockers. The rank order of inhibition by these compds. was consistent with glutamate uptake assay results reported previously. Thus, the [3H]ETB-TBOA binding assay will be useful to screen novel EAAT ligands for all EAAT subtypes.
IT 864937-05-3P
RL: ARG (Analytical reagent use); PKT (Pharmacokinetics); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(characterization of tritium-labeled analog of L-threo-β-benzyloxyaspartate binding to glutamate transporters)
RN 864937-05-3 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(ethyl-1,2-t2)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2006:656062 CAPLUS
DOCUMENT NUMBER: 145:124841
TITLE: Preparation of β-benzyloxyaspartic acid derivatives as affinity-column ligands and glutamic acid transporter inhibitors
INVENTOR(S): Shimamoto, Keiko
PATENT ASSIGNEE(S): Suntory Limited, Japan
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006070737	A1	20060706	WO 2005-JP23773	20051226
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
JP 2006182696	A	20060713	JP 2004-377557	20041227
JP 4008446	B2	20071114		
EP 1849766	A1	20071031	EP 2005-820230	20051226
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
US 20080070321	A1	20080320	US 2007-794124	20070626
US 7670784	B2	20100302		

PRIORITY APPLN. INFO.: JP 2004-377557 A 20041227
WO 2005-JP23773 W 20051226

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 145:124841
G1

EXR: Michael Barker

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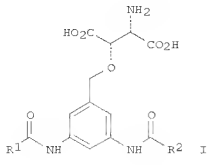
L6 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



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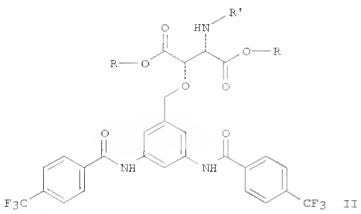


II

AB Title compds. I [R1 = (un)substituted aromatic group; R2 = (un)substituted linear or branched aliphatic group optionally having nitrogen or oxygen in the chain, (un)substituted aromatic group] and salts thereof were prepared For example, treatment of compound II [R = tert-butyl; R' = tert-butoxycarbonyl] with trifluoroacetic acid afforded compound II [R, R' = H] trifluoroacetic acid salt in 84% yield. In glutamic acid uptake inhibition assays, IC50 values of compound II [R, R' = H]·CF3CO2H for EAAT2 and EAAT3 were 1.3 and 0.46 nM, resp. A method of purifying or detecting an L-glutamic acid transporter using compds. I is provided.

IT 896712-90-6P 896712-92-8P 896712-94-0P
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of β-benzyloxyaspartic acid derivs. as affinity-column ligands and glutamic acid transporter inhibitors)

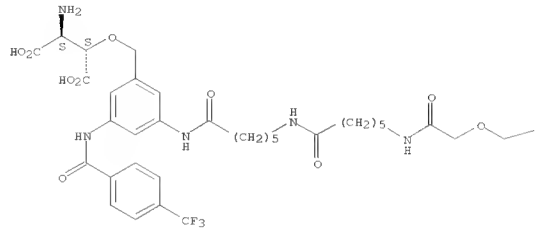
RN 896712-90-6 CAPLUS
CN L-Aspartic acid, 3-[[3-[(28-amino-1,8,15-trioxo-17,20,23,26-tetraoxa-7,14-diazaoctacos-1-yl)amino]-5-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

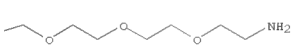
CRN 896712-89-3
CMF C41 H59 F3 N6 O13

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



CM 2

CRN 76-05-1
CMF C2 H F3 O2

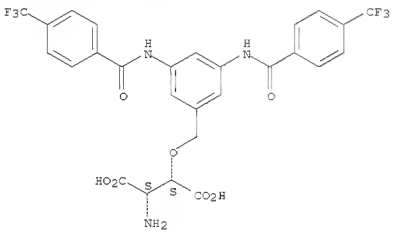
L6 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)

RN 896712-92-8 CAPLUS
CN L-Aspartic acid, 3-[[3,5-bis[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 896712-91-7
CMF C27 H21 F6 N3 O7

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

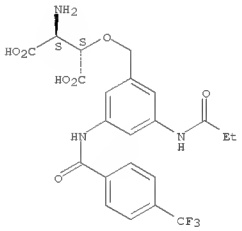
RN 896712-94-0 CAPLUS
CN L-Aspartic acid, 3-[[3-[(1-oxopropyl)amino]-5-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

L6 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)

CRN 896712-93-9
CMF C22 H22 F3 N3 O7

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

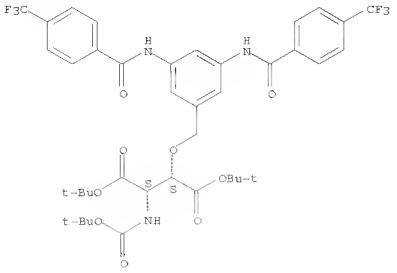
IT 896713-01-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of β-benzyloxyaspartic acid derivs. as affinity-column ligands and glutamic acid transporter inhibitors)

RN 896713-01-2 CAPLUS
CN L-Aspartic acid, 3-[[3,5-bis[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-N-[(1,1-dimethylethoxy)carbonyl]-, bis(1,1-dimethylethyl) ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10593034

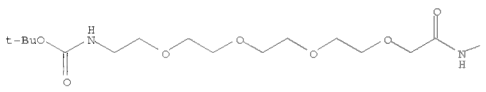
L6 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



IT 896713-00-1P 896713-02-3P 896713-03-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of β-benzyloxyaspartic acid derivs. as affinity-column ligands and glutamic acid transporter inhibitors)
RN 896713-00-1 CAPLUS
CN L-Aspartic acid, N-[(1,1-dimethylethoxy)carbonyl]-3-[[3-[(32,32-dimethyl-1,8,15,30-tetraoxo-17,20,23,26,31-pentaoxa-7,14,29-triazatritriacont-1-yl)amino]-5-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, bis(1,1-dimethylethyl) ester, (3S)- (9CI) (CA INDEX NAME)

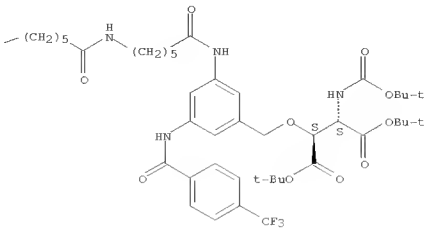
Absolute stereochemistry. Rotation (+).

PAGE 1-A



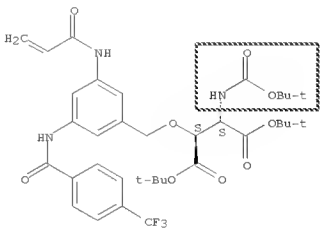
L6 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)

PAGE 1-B



RN 896713-02-3 CAPLUS
CN L-Aspartic acid, N-[(1,1-dimethylethoxy)carbonyl]-3-[[3-[(1-oxo-2-propenyl)amino]-5-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, bis(1,1-dimethylethyl) ester, (3S)- (9CI) (CA INDEX NAME)

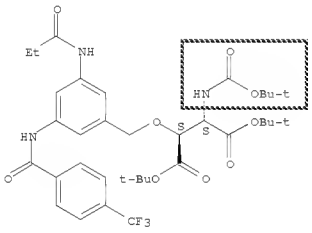
Absolute stereochemistry.



RN 896713-03-4 CAPLUS
CN L-Aspartic acid, N-[(1,1-dimethylethoxy)carbonyl]-3-[[3-[(1-oxopropyl)amino]-5-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, bis(1,1-dimethylethyl) ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

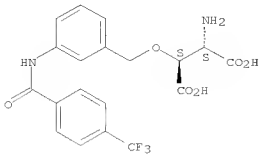
L6 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2006:129293 CAPLUS
DOCUMENT NUMBER: 144:324958
TITLE: Elucidation of glutamate transporter functions using selective inhibitors
AUTHOR(S): Shimamoto, Keiko
CORPORATE SOURCE: Suntory Institute for Bioorganic Research, 1-1-1 Wakayamadai, Shimamoto-cho, Mishima-gun, Osaka, 618-8503, Japan
SOURCE: Shinkei Kenkyu no Shinpo (2005), 49(6), 850-854
CODEN: SKNSAF; ISSN: 0001-8724
PUBLISHER: Igaku Shoin Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review. L-Glutamate is the major excitatory neurotransmitter in the mammalian central nervous system(CNS). To terminate glutamate receptor activation and to protect neurons from excitotoxicity, extracellular glutamate concns. are strictly controlled by sodium dependent glutamate transporters (excitatory amino acid transporters 1-5 : EAATs1-5) located in nerve endings and surrounding glia cells. Selective and potent inhibitors have served as important exptl. tools to identify the physiol. roles of transporters in the regulation of synaptic transmission or in the pathogenesis of neurol. diseases. A pharmacol. useful probe, threo-β-benzyloxyaspartate (DL-TBOA) which functions as a non-transportable blocker for all subtypes of EAATs, has emerged from modification of a known inhibitor threo-β-hydroxyaspartate (THA). Non-transportable blockers are indispensable because, unlike substrates, they do not cause heteroexchange. By comparing the effects of substrates and non-transportable blockers, physiol. roles of EAATs have been revealed. EAATs not only remove transmitter from synaptic clefts but also actively modulate neurotransmission. Moreover, higher affinity ligands have been developed as novel pharmacol. tools. TBOA analogs possessing a bulky substituent on their benzene ring significantly inhibited labeled glutamate uptake, the most potent of compound being (2S, 3S)-3-(3-[4-(tri-fluoromethyl) benzoyl-amino] benzyloxy] aspartate (TFB-TBOA). TFB-TBOA is genuinely non-transportable at ED and showed no effects on glutamate receptors. TFB-TBOA would be a suitable lead compound for designing functionalized ligands from the perspective of its markedly high affinity for EAAT proteins.
IT 480439-73-4, TFB-TBOA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(elucidation of glutamate transporter functions using selective inhibitors)
RN 480439-73-4 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

EXR: Michael Barker

10593034

L6 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



L6 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2006:58482 CAPLUS
DOCUMENT NUMBER: 144:429643
TITLE: Roles of glial glutamate transporters in shaping EPSCs at the climbing fiber-Purkinje cell synapses
AUTHOR(S): Takatsuru, Yusuke; Takayasu, Yukihiro; Iino, Masae; Nikkuni, Osamu; Ueda, Yuto; Tanaka, Kohichi; Ozawa, Seiji
CORPORATE SOURCE: Department of Neurophysiology, Gunma University Graduate School of Medicine, Maebashi, Gunma, 371-8511, Japan
SOURCE: Neuroscience Research (Amsterdam, Netherlands) (2006), 54(2), 140-148
CODEN: NERADN; ISSN: 0168-0102
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

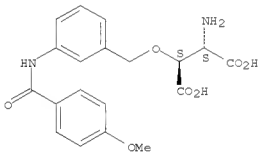
AB Glial glutamate transporters, GLAST and GLT-1, are co-localized in processes of Bergmann glia (BG) wrapping excitatory synapses on Purkinje cells (PCs). Although GLAST is expressed six-fold more abundantly than GLT-1, no change is detected in the kinetics of climbing fiber (CF)-mediated excitatory postsynaptic currents (CF-EPSCs) in PCs in GLAST(-/-) mice compared to the wild-type mice (WT). Here we aimed to clarify the mechanism(s) underlying this unexpected finding using a selective GLT-1 blocker, dihydrokainate (DHK), and a novel antagonist of glial glutamate transporter, (2S,3S)-3-[3-(4-methoxybenzoylamino)benzyloxy]aspartate (PMB-TBOA). In the presence of cyclothiazide (CTZ), which attenuates the desensitization of AMPA receptors, DHK prolonged the decay time constant (τw) of CF-EPSCs in WT, indicating that GLT-1 plays a partial role in the removal of glutamate. The application of 100 nM PMB-TBOA, which inhibited CF-mediated transporter currents in BG by .apprx.80%, caused no change in τ w in WT in the absence of CTZ, whereas it prolonged τ w in the presence of CTZ. This prolonged value of τw was similar to that in GLAST(-/-) mice in the presence of CTZ. These results indicate that glial glutamate transporters can apparently retain the fast decay kinetics of CF-EPSCs if a small proportion (.apprx.20%) of functional transporters is preserved.

IT 480439-66-5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(glial glutamate transporter antagonist (2S,3S)-3-[3-(4-methoxybenzoylamino)benzyloxy]aspartate inhibited CF-mediated transporter currents in Bergmann glia and prolonged decay time constant in presence of cyclothiazide in GLAST(-/-) mouse)

RN 480439-66-5 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-methoxybenzoyl)amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN

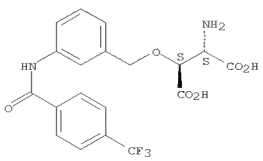
ACCESSION NUMBER: 2006:24201 CAPLUS
DOCUMENT NUMBER: 144:142897
TITLE: Facilitative effect of a glutamate transporter inhibitor (2S,3S)-3-{3-[4-(trifluoromethyl)benzoylamino]benzyloxy}aspartate on the expression of methamphetamine-induced behavioral sensitization in rats
AUTHOR(S): Fujio, Mayumi; Nakagawa, Takayuki; Suzuki, Yuichi; Satoh, Masamichi; Kaneko, Shuji
CORPORATE SOURCE: Department of Molecular Pharmacology, Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan
SOURCE: Journal of Pharmacological Sciences (Tokyo, Japan) (2005), 99(4), 415-418
CODEN: JPSTGJ; ISSN: 1347-8613
PUBLISHER: Japanese Pharmacological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We examined the effects of a potent glutamate transporter inhibitor, (2S,3S)-3-{3-[4-(trifluoromethyl)benzoylamino]benzyloxy}aspartate (TFB-TBOA), on the expression of methamphetamine-induced behavioral sensitization in rats. Rats were i.p. treated with 2 mg/kg methamphetamine for 5 days and then challenged with 1 mg/kg methamphetamine. Intracerebroventricular administration of TFB-TBOA (0.1 nmol) 10 min before the challenge significantly facilitated the expression of behavioral sensitization. It had no effect on the locomotor activation elicited by the challenge with methamphetamine in repeated-saline-treated (non-sensitized) rats. These results suggest that central glutamate transporters may play an inhibitory role in the expression of behavioral sensitization to methamphetamine.

IT 480439-73-4
RL: PAC (Pharmacological activity); BIOL (Biological study)
(facilitative effect of a glutamate transporter inhibitor {[(trifluoromethyl)benzoylamino]benzyloxy}aspartate on expression of methamphetamine-induced behavioral sensitization in rats)

RN 480439-73-4 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD

EXR: Michael Barker

10593034

INSTANT APPLICATION

L6 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
(1 CITINGS)
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

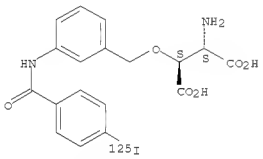
L6 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2005:1042190 CAPLUS
DOCUMENT NUMBER: 143:306541
TITLE: Preparation of radiolabeled 3-[3-(benzoylamino)benzyloxy]aspartic acid derivatives as glutamate transporter inhibitors
INVENTOR(S): Shimamoto, Keiko; Saji, Hideo; Kuge, Yuji; Ueda, Masashi; Satoh, Masamichi; Nakagawa, Takayuki
PATENT ASSIGNEE(S): Suntory Limited, Japan
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005090268	A1	20050929	WO 2005-JP5600	20050318
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1732864	A1	20061220	EP 2005-721527	20050318
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007529412	T	20071025	JP 2006-523410	20050318
US 20080248485	A1	20081009	US 2006-593034	20060915
PRIORITY APPLN. INFO.:			JP 2004-79116	A 20040318
			WO 2005-JP5600	W 20050318

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 143:306541; MARPAT 143:306541
AB The invention provides a radiolabeled ligand which is highly selective and potent for glutamate transporters and is usable in specifically detecting the glutamate transporter. Specifically, the invention provides 3-[3-(benzoylamino)benzyloxy]aspartic acid (BzA-TBOA) having a radioactive substituent at the p-position of the benzoyl group, as well as esters or salts. Thus, [125I]I-BzA-TBOA was prepared from N,O-protected A-TBOA by acylation with 4-bromobenzoyl chloride, tributylstannylation, substitution reaction with Na125I, and deprotection. Glutamate transporter inhibitory activity data are tabulated for compds. of the invention.

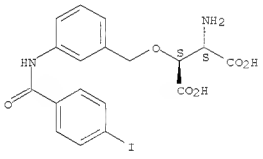
L6 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
IT 864936-98-1P 864936-99-2P 864937-01-9P
864937-04-2P
RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of radiolabeled [(benzoylamino)benzyloxy]aspartic acid derivs.
as glutamate transporter inhibitors)
RN 864936-98-1 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(iodo-125I)benzoyl]amino]phenyl]methoxy]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 864936-99-2 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-iodobenzoyl)amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

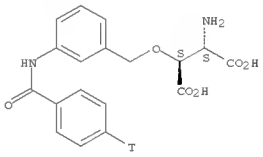
Absolute stereochemistry.



RN 864937-01-9 CAPLUS
CN L-Aspartic acid, 3-[[3-(benzoyl-4-t-amino)phenyl]methoxy]-, (3S)- (9Cl) (CA INDEX NAME)

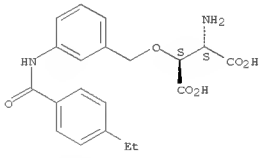
Absolute stereochemistry.

L6 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



RN 864937-04-2 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-ethylbenzoyl)amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



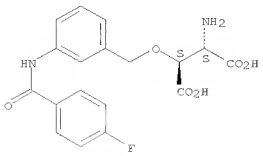
IT 480439-71-2 480439-73-4 864937-05-3D,
tritium-labeled
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of radiolabeled [(benzoylamino)benzyloxy]aspartic acid derivs.
as glutamate transporter inhibitors)
RN 480439-71-2 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-fluorobenzoyl)amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

EXR: Michael Barker

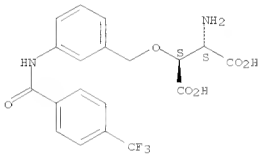
10593034

L6 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



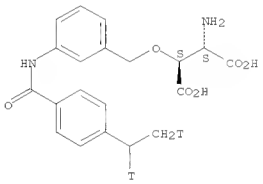
RN 480439-73-4 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



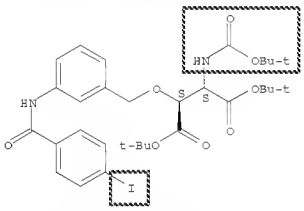
RN 864937-05-3 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(ethyl-1,2-t2)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



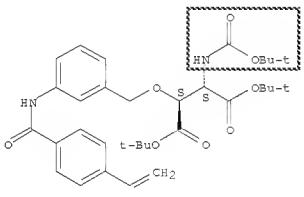
L6 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)

Absolute stereochemistry.



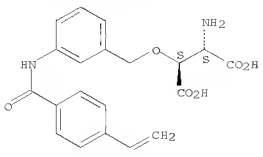
RN 864937-02-0 CAPLUS
CN L-Aspartic acid, N-[(1,1-dimethylethoxy)carbonyl]-3-[[3-[(4-ethenylbenzoyl)amino]phenyl]methoxy]-, bis(1,1-dimethylethyl) ester, (3S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 864937-03-1 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-ethenylbenzoyl)amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

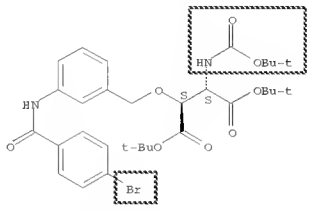


L6 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)

IT 864936-96-9P 864936-97-0P 864937-00-8P
864937-02-0P 864937-03-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of radiolabeled [(benzoylamino)benzyloxy]aspartic acid derivs.
as glutamate transporter inhibitors)

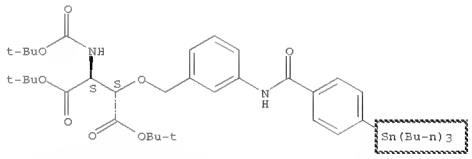
RN 864936-96-9 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-bromobenzoyl)amino]phenyl]methoxy]-N-[(1,1-dimethylethoxy)carbonyl]-, bis(1,1-dimethylethyl) ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 864936-97-0 CAPLUS
CN L-Aspartic acid, N-[(1,1-dimethylethoxy)carbonyl]-3-[[3-[[4-(tributylstannyl)benzoyl]amino]phenyl]methoxy]-, bis(1,1-dimethylethyl) ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 864937-00-8 CAPLUS
CN L-Aspartic acid, N-[(1,1-dimethylethoxy)carbonyl]-3-[[3-[(4-iodobenzoyl)amino]phenyl]methoxy]-, bis(1,1-dimethylethyl) ester, (3S)-
(9CI) (CA INDEX NAME)

L6 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

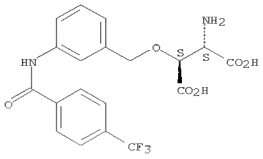
EXR: Michael Barker

10593034

L6 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2005:299120 CAPLUS
DOCUMENT NUMBER: 142:442183
TITLE: A novel L-glutamate transporter inhibitor reveals endogenous D-aspartate homeostasis in rat pheochromocytoma MPT1 cells
AUTHOR(S): Koyama, Hayato; Sekine, Masae; Furuchi, Takemitsu; Katane, Masumi; Nimura, Noriyuki; Shimamoto, Keiko; Nakajima, Terumi; Homma, Hiroshi
CORPORATE SOURCE: School of Pharmaceutical Sciences, Kitasato University, Minato-ku, Tokyo, 108-8641, Japan
SOURCE: Life Sciences (2005), 76(25), 2933-2944
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We previously reported for the first time that D-aspartate (D-Asp) is biosynthesized by cultured mammalian cells such as pheochromocytoma (PC)12 cells and its subclone MPT1 (FEBS Lett. 434 (1998) 231, Arch. Biochem. Biophys. 404 (2002) 92). We speculated that D-Asp levels in the intra- and extracellular spaces of the cultured cells are maintained in a dynamic state of homeostasis. To test this here, we utilized a novel and potent L-Glu transporter inhibitor, (2S,3S)-3-{3-[4-(trifluoromethyl)benzyloylamino]benzyloxy}aspartate (TFB-TBOA). This inhibitor proved to be a genuine nontransportable blocker of the transporter even during long periods of culture. Use of this inhibitor with MPT1 cells confirmed that D-Asp levels are in a dynamic steady state where it is constantly released into the extracellular space by a yet undefined mechanism as well as being constantly and intensively taken up by the cells via the L-Glu transporter. We estimated the rate with which D-Asp is constitutively released from MPT1 cells is approx. 3.8 pmol/h/1 × 105 cells.
IT 480439-73-4
RL: BUU (Biological use, unclassified); PAC (Pharmacological activity); BIOL (Biological study); USES (Uses)
(glutamate transporter inhibitor reveals endogenous D-aspartate homeostasis in rat pheochromocytoma MPT1 cells)
RN 480439-73-4 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)

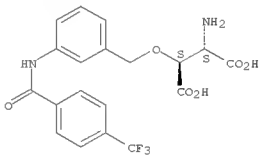


OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2005:214287 CAPLUS
DOCUMENT NUMBER: 143:146338
TITLE: Effects of a novel glutamate transporter blocker, (2S,3S)-3-{3-[4-(trifluoromethyl)benzoylamino]benzyloxy}aspartate (TFB-TBOA), on activities of hippocampal neurons
AUTHOR(S): Tsukada, Shota; Iino, Masae; Takayasu, Yukihiro; Shimamoto, Keiko; Ozawa, Seiji
CORPORATE SOURCE: Department of Neurophysiology, Gunma University Graduate School of Medicine, 3-39-22 Showa-machi, Maebashi, Gunma, 371-8511, Japan
SOURCE: Neuropharmacology (2005), 48(4), 479-491
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Glutamate transporters rapidly take up synaptically released glutamate and maintain the glutamate concentration in the synaptic cleft at a low level. (2S,3S)-3-{3-[4-(trifluoromethyl)benzoylamino]benzyloxy}aspartate (TFB-TBOA) is a novel glutamate transporter blocker that potently suppresses the activity of glial transporters. TFB-TBOA inhibited synaptically activated transporter currents (STCs) in astrocytes in the stratum radiatum in rat hippocampal slices in a dose-dependent manner with an IC50 of 13 nM, and reduced them to approx. 10% of the control at 100 nM. We investigated the effects of TFB-TBOA on glutamatergic synaptic transmission and cell excitability in CA1 pyramidal cells. TFB-TBOA (100 nM) prolonged the decay of N-methyl--aspartic acid receptor (NMDAR)-mediated excitatory postsynaptic currents (EPSCs), whereas it prolonged that of α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR)-mediated EPSCs only when the desensitization of AMPARs was reduced by cyclothiazide (CTZ). Furthermore, long-term application of TFB-TBOA induced spontaneous epileptiform discharges with a continuous depolarization shift of membrane potential. These epileptiform activities were mainly attributed to NMDAR activation. Even after pharmacol. block of NMDARs, however, TFB-TBOA induced similar changes by activating AMPARs in the presence of CTZ. Thus, the continuous uptake of synaptically released glutamate by glial transporters is indispensable for protecting hippocampal neurons from glutamate receptor-mediated hyperexcitabilities.
IT 480439-73-4, TFB-TBOA
RL: PAC (Pharmacological activity); BIOL (Biological study)
(effects of a novel glutamate transporter blocker, (2S,3S)-3-{3-[4-(trifluoromethyl)benzoylamino]benzyloxy}aspartate (TFB-TBOA), on activities of hippocampal neurons)
RN 480439-73-4 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

EXR: Michael Barker

10593034

L6 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2004:469790 CAPLUS
DOCUMENT NUMBER: 141:184585
TITLE: Synthesis of carbamate-type caged derivatives of a novel glutamate transporter blocker
AUTHOR(S): Takaoka, Kiyo; Tatsu, Yoshiro; Yumoto, Noboru; Nakajima, Terumi; Shimamoto, Keiko
CORPORATE SOURCE: Suntory Institute for Bioorganic Research, 1-1-1 Wakayamadai, Osaka, Shimamoto, 618-8503, Japan
SOURCE: Bioorganic & Medicinal Chemistry (2004), 12(13), 3687-3694
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:184585

AB L-threo-β-Benzyloxyaspartate (L-TBOA) and (2S,3S)-3-{3-[4-(trifluoromethyl)benzoylamino]benzyloxy}aspartate (L-TFB-TBOA) are potent nontransportable blockers for glutamate transporters. The authors synthesized a carbamate-type coumarin derivative of L-TBOA (3a) as a caged blocker and compared 3a with the corresponding ester-type analogs 1. The carbamate 3a was less sensitive to photolysis than the ester 1 but was more stable in the aqueous solution. The [6,7-bis(carboxymethoxy)-coumarin-4-yl]methylcarbonyl (BCMCMC) group exhibited good results both in photoreactivity and stability. Therefore, the authors examined photolysis of N-BCMCMC-TBOA and N-BCMCMC-TFB-TBOA, which immediately released blockers to show glutamate uptake inhibition.

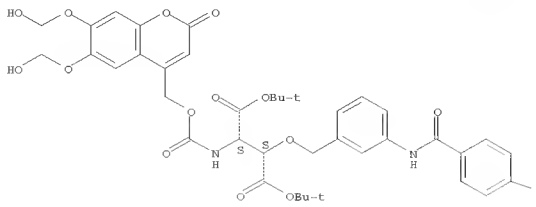
IT 737830-26-1P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of carbamate-type caged derivs. of novel glutamate transporter blocker)

RN 737830-26-1 CAPLUS
CN L-Aspartic acid, N-[[[6,7-bis(hydroxymethoxy)-2-oxo-2H-1-benzopyran-4-yl]methoxy]carbonyl]-3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, bis(1,1-dimethylethyl) ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)

PAGE 1-A



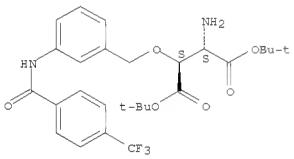
PAGE 1-B

IT 737830-21-6P 737830-22-7P 811412-49-4P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of carbamate-type caged derivs. of novel glutamate transporter blocker)

RN 737830-21-6 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, bis(1,1-dimethylethyl) ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

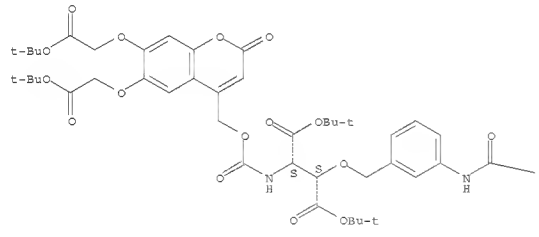
L6 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



RN 737830-22-7 CAPLUS
CN L-Aspartic acid, N-[[[6,7-bis[2-(1,1-dimethylethoxy)-2-oxoethoxy]-2-oxo-2H-1-benzopyran-4-yl]methoxy]carbonyl]-3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, bis(1,1-dimethylethyl) ester, (3S)- (9CI) (CA INDEX NAME)

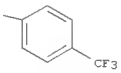
Absolute stereochemistry.

PAGE 1-A



L6 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)

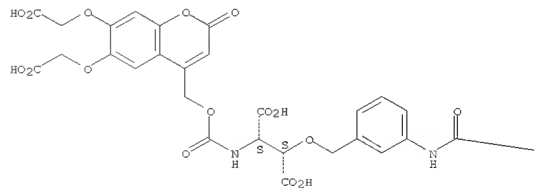
PAGE 1-B



RN 811412-49-4 CAPLUS
CN L-Aspartic acid, N-[[[6,7-bis(carboxymethoxy)-2-oxo-2H-1-benzopyran-4-yl]methoxy]carbonyl]-3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A

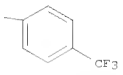


EXR: Michael Barker

10593034

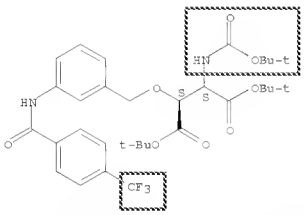
L6 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)

PAGE 1-B



IT 737830-20-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of carbamate-type caged derivs. of novel glutamate transporter blocker)
RN 737830-20-5 CAPLUS
CN L-Aspartic acid, N-[(1,1-dimethylethoxy)carbonyl]-3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, bis(1,1-dimethylethyl) ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



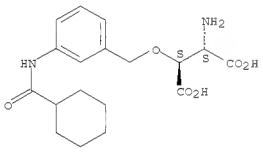
OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2004:292674 CAPLUS
DOCUMENT NUMBER: 141:16890
TITLE: Characterization of novel L-threo-β-benzyloxyaspartate derivatives, potent blockers of the glutamate transporters
AUTHOR(S): Shimamoto, Keiko; Sakai, Ryuichi; Takaoka, Kiyo; Yumoto, Noboru; Nakajima, Terumi; Amara, Susan G.; Shigeri, Yasushi
CORPORATE SOURCE: Suntory Institute for Bioorganic Research, Osaka, 618-8503, Japan
SOURCE: Molecular Pharmacology (2004), 65(4), 1008-1015
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Nontransportable blockers of the glutamate transporters are important tools for investigating mechanisms of synaptic transmission. DL-threo-β-Benzyloxyaspartate (DL-TBOA) is a potent blocker of all subtypes of the excitatory amino acid transporters (EAATs). We characterized novel L-TBOA analogs possessing a substituent on their resp. benzene rings. The analogs significantly inhibited labeled glutamate uptake, the most potent of which was (2S,3S)-3-{3-[4-(trifluoromethyl)benzoylamino]benzyloxy}aspartate (TFB-TBOA). In an uptake assay using cells transiently expressing EAATs, the IC50 values of TFB-TBOA for EAAT1, EAAT2, and EAAT3 were 22, 17, and 300 nM, resp. TFB-TBOA was significantly more potent at inhibiting EAAT1 and EAAT2 compared with L-TBOA (IC50 values for EAAT1-3 were 33, 6.2, and 15 μM, resp.). Electrophysiol. analyses revealed that TBOA analogs block the transport-associated currents in all five EAAT subtypes and also block leak currents in EAAT5. The rank order of the analogs for potencies at inhibiting substrate-induced currents was identical to that observed in the uptake assay. However, the kinetics of TFB-TBOA differed from the kinetics of L-TBOA, probably because of the strong binding affinity. Notably, TFB-TBOA did not affect other representative neurotransmitter transporters or receptors, including ionotropic and metabotropic glutamate receptors, indicating that it is highly selective for EAATs. Moreover, intracerebroventricular administration of the TBOA analogs induced severe convulsive behaviors in mice, probably because of the accumulation of glutamate. Taken together, these findings indicate that novel TBOA analogs, especially TFB-TBOA, should serve as useful tools for elucidating the physiol. roles of the glutamate transporters.

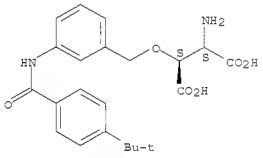
IT 479690-56-7 479690-57-8 480439-63-2
480439-64-3 480439-65-4 480439-66-5
480439-67-6 480439-68-7 480439-69-8
480439-70-1 480439-71-2 480439-72-3
480439-73-4
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(characterization of novel L-threo-β-benzyloxyaspartate derivs., potent blockers of glutamate transporters)
RN 479690-56-7 CAPLUS
CN L-Aspartic acid, 3-[[3-[(cyclohexylcarbonyl)amino]phenyl]methoxy]-, (3S)-
(CA INDEX NAME)

Absolute stereochemistry.



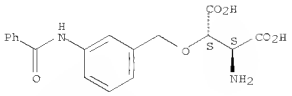
RN 479690-57-8 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 480439-63-2 CAPLUS
CN L-Aspartic acid, 3-[[3-(benzoylamino)phenyl]methoxy]-, (3S)- (CA INDEX NAME)

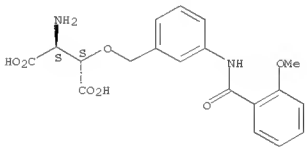
Absolute stereochemistry.



RN 480439-64-3 CAPLUS
CN L-Aspartic acid, 3-[[3-[(2-methoxybenzoyl)amino]phenyl]methoxy]-, (3S)-

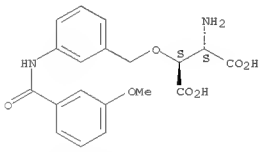
L6 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
(CA INDEX NAME)

Absolute stereochemistry.



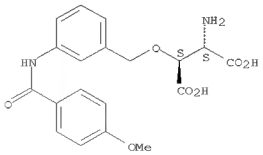
RN 480439-65-4 CAPLUS
CN L-Aspartic acid, 3-[[3-[(3-methoxybenzoyl)amino]phenyl]methoxy]-, (3S)-
(CA INDEX NAME)

Absolute stereochemistry.



RN 480439-66-5 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-methoxybenzoyl)amino]phenyl]methoxy]-, (3S)-
(CA INDEX NAME)

Absolute stereochemistry.



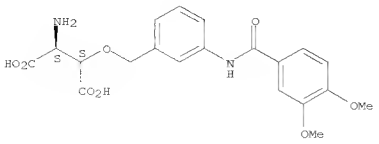
RN 480439-67-6 CAPLUS
CN L-Aspartic acid, 3-[[3-[(3,4-dimethoxybenzoyl)amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

EXR: Michael Barker

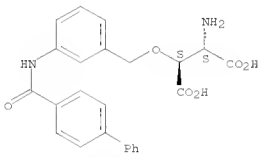
10593034

L6 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



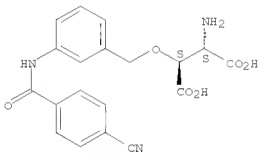
RN 480439-68-7 CAPLUS
CN L-Aspartic acid, 3-[[3-[([1,1'-biphenyl]-4-ylcarbonyl)amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



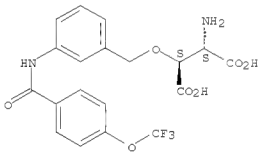
RN 480439-69-8 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-cyanobenzoyl)amino]phenyl]methoxy]-, (3S)-(CA
INDEX NAME)

Absolute stereochemistry.



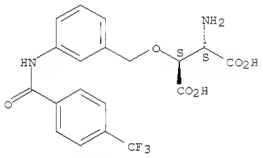
RN 480439-70-1 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-nitrobenzoyl)amino]phenyl]methoxy]-, (3S)-(CA

L6 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



RN 480439-73-4 CAPLUS
CN L-Aspartic acid,
3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-
, (3S)- (CA INDEX NAME)

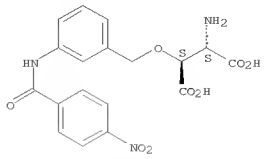
Absolute stereochemistry.



OS.CITING REF COUNT: 44 THERE ARE 44 CAPLUS RECORDS THAT CITE THIS RECORD (44 CITINGS)
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

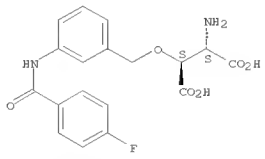
L6 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
INDEX NAME)

Absolute stereochemistry.



RN 480439-71-2 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-fluorobenzoyl)amino]phenyl]methoxy]-, (3S)-(CA INDEX NAME)

Absolute stereochemistry.



RN 480439-72-3 CAPLUS
CN L-Aspartic acid,
3-[[3-[[4-(trifluoromethoxy)benzoyl]amino]phenyl]methoxy]-
, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN
ACCESSION NUMBER: 2003:5966 CAPLUS
DOCUMENT NUMBER: 138:72990
TITLE: Preparation of β-(aminobenzyloxy)aspartate derivatives as glutamate transporter inhibitors
INVENTOR(S): Shimamoto, Keiko
PATENT ASSIGNEE(S): Suntory Limited, Japan
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000638	A1	20030103	WO 2002-JP6286	20020624
W: AU, BR, CA, CN, IL, JP, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
AU 2002345364	A1	20030108	AU 2002-345364	20020624
EP 1397370	A1	20040317	EP 2002-743696	20020624
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
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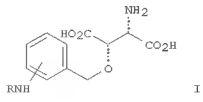
JP 4542336	B2	20100915		
US 20040242652	A1	20041202	US 2004-481237	20040719
US 7247652	B2	20070724		
US 20070238783	A1	20071011	US 2007-808970	20070614
US 7666906	B2	20100223		

PRIORITY APPLN. INFO.: JP 2001-190022 A 20010622
WO 2002-JP6286 W 20020624
US 2004-481237 A3 20040719

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 138:72990; MARPAT 138:72990
GI



I

AB L-Threo-β-benzyloxyaspartate derivs. I [R = H, (un)substituted acyl, an amino acid- or biotin-derived group] or their salts were prepared for binding to affinity column chromatog. carriers as ligands of glutamate transporter proteins. Thus, I (R = m-H2NCH2CH2CONH) (AA-TBOA) was prepared
by a multistep synthesis starting with the reaction of

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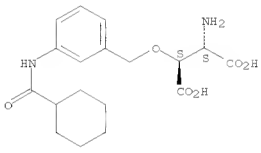
L6 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
(2S,3R)-[3-(benzyloxymethyl)oxiranyl]methyl p-nitrobenzoate with benzoyl isocyanate. The inhibitory effect of AA-TBOA was detd. to be IC50 = 2.1 ± 0.1 μM and 7.9 ± 0.76 μM, resp., for uptake of (14)glutamate by human EAAT2 or EAAT3 stably expressed on MDCK cells or transiently expressed on COS-1 cells.
IT 479690-56-7P, CHexA-TBOA 479690-57-8P, TBu-BzA-TBOA
479690-58-9P 480439-63-2P, BzA-TBOA
480439-64-3P, o-MeO-BzA-TBOA 480439-65-4P,
m-MeO-BzA-TBOA 480439-66-5P, p-MeO-BzA-TBOA
480439-67-6P, DiMeO-BzA-TBOA 480439-68-7P, Ph-Bza-TBOA
480439-69-8P, CN-Bza-TBOA 480439-70-1P, NO2-Bza-TBOA
480439-71-2P, F-Bza-TBOA 480439-72-3P, OCF3-Bza-TBOA
480439-73-4P, CF3-Bza-TBOA 480439-74-5P, OHex-Bza-TBOA
480439-76-7P, A-PenO-BzA-TBOA 480439-77-8P,
BioA-PenO-BzA-TBOA
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (aminobenzyloxy)aspartate derivs. as glutamate transporter
inhibitors)
RN 479690-56-7 CAPLUS
CN L-Aspartic acid, 3-[[3-[(cyclohexylcarbonyl)amino]phenyl]methoxy]-, (3S)-
(CA INDEX NAME)

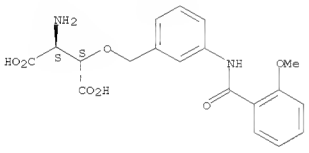
Absolute stereochemistry.



RN 479690-57-8 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

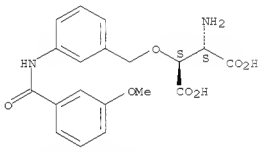
Absolute stereochemistry.

L6 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



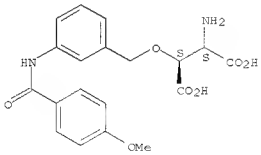
RN 480439-65-4 CAPLUS
CN L-Aspartic acid, 3-[[3-[(3-methoxybenzoyl)amino]phenyl]methoxy]-, (3S)-
(CA INDEX NAME)

Absolute stereochemistry.



RN 480439-66-5 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-methoxybenzoyl)amino]phenyl]methoxy]-, (3S)-
(CA INDEX NAME)

Absolute stereochemistry.



RN 480439-67-6 CAPLUS
CN L-Aspartic acid, 3-[[3-[(3,4-dimethoxybenzoyl)amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

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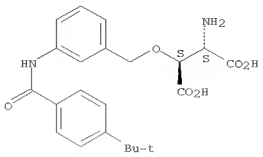
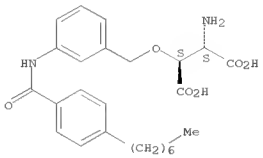
L6 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



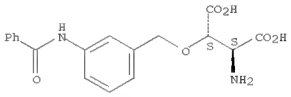
RN 479690-58-9 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-heptylbenzoyl)amino]phenyl]methoxy]-, (3S)-
(CA INDEX NAME)

Absolute stereochemistry.



RN 480439-63-2 CAPLUS
CN L-Aspartic acid, 3-[[3-(benzoylamino)phenyl]methoxy]-, (3S)- (CA INDEX NAME)

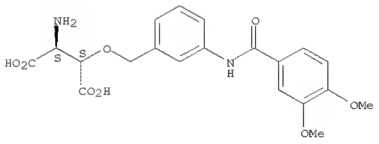
Absolute stereochemistry.



RN 480439-64-3 CAPLUS
CN L-Aspartic acid, 3-[[3-[(2-methoxybenzoyl)amino]phenyl]methoxy]-, (3S)-
(CA INDEX NAME)

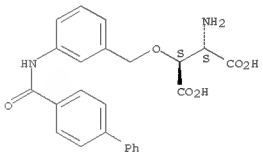
Absolute stereochemistry.

L6 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



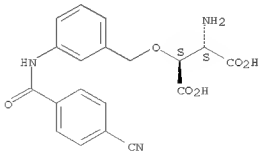
RN 480439-68-7 CAPLUS
CN L-Aspartic acid, 3-[[3-[([1,1'-biphenyl]-4-ylcarbonyl)amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 480439-69-8 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-cyanobenzoyl)amino]phenyl]methoxy]-, (3S)-
(CA
INDEX NAME)

Absolute stereochemistry.



RN 480439-70-1 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-nitrobenzoyl)amino]phenyl]methoxy]-, (3S)-
(CA
INDEX NAME)

Absolute stereochemistry.

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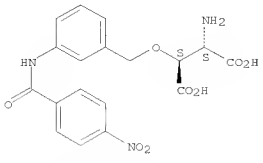
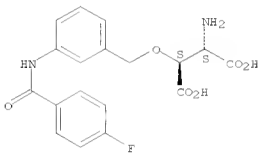
L6 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



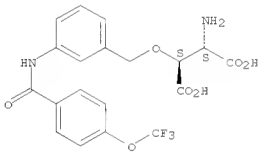
RN 480439-71-2 CAPLUS
CN L-Aspartic acid, 3-[[3-[(4-fluorobenzoyl)amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 480439-72-3 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethoxy)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

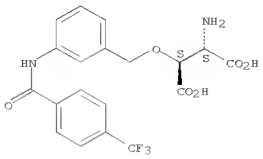
Absolute stereochemistry.



RN 480439-73-4 CAPLUS

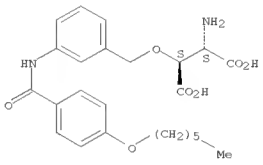
L6 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
CN L-Aspartic acid, 3-[[3-[[4-(trifluoromethyl)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 480439-74-5 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-(hexyloxy)benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

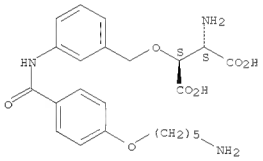
Absolute stereochemistry.



RN 480439-76-7 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-[(5-aminopentyl)oxy]benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)



RN 480439-77-8 CAPLUS
CN L-Aspartic acid, 3-[[3-[[4-[[5-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]pentyl]oxy]benzoyl]amino]phenyl]methoxy]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

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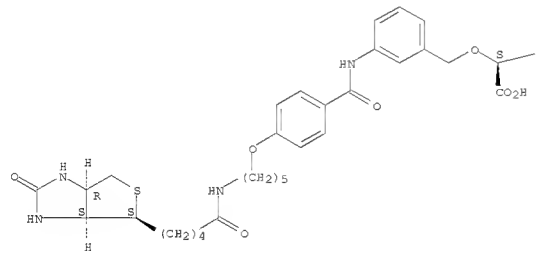

PAGE 1-B

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L6 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2011 ACS on STN (Continued)
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